

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference X16538	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/US2005/007507	International filing date (day/month/year) 09/03/2005	(Earliest) Priority Date (day/month/year) 22/03/2004
Applicant ELI LILLY AND COMPANY		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ Certain claims were found unsearchable (See Box II).3. ☐ Unity of invention is lacking (see Box III).4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings**,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

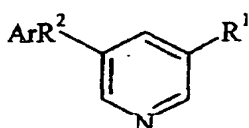
☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☐ none of the figures is to be published with the abstract.

Box No. IV Text of the abstract (Continuation of item 5 of the first sheet)

The present invention is directed toward pyridyl derivatives of formula (I) as antagonists of the mGlu5 receptor. As such the compounds may be useful for treatment or prevention of disorders remedied by antagonism of the mGlu5 receptor.



(I)

wherein

Ar is phenyl or naphthyl each of which may be substituted by one or more C_1 - C_4 alkyl, C_1 - C_4 alkoxy, C_1 - C_5 acyl, halo, amino, nitro, cyano, hydroxy, C_1 - C_5 acylamino, C_1 - C_4 alkylsulfonylamino, mono-, di- or trifluorinated C_1 - C_3 alkyl, substituents which may be the same or different and may bear a CONH_2 , CONHCH_3 , $\text{CON}(\text{CH}_3)_2$, CO_2H , CO_2CH_3 , OCF_3 , $\text{CH}_2\text{NHCOCH}_3$, CH_2NH_2 , $\text{CH}_2\text{N}(\text{CH}_3)_2$, CH_2CN , CH_2OH , $\text{CH}_2\text{NHSO}_2\text{CH}_3$, $\text{CH}_2\text{N}(\text{CH}_3)(\text{CH}_2)_2\text{CN}$, $\text{CH}_2\text{N}(\text{CH}_3)\text{CH}(\text{CH}_3)_2$, $\text{CH}_2\text{NHCH}(\text{CH}_3)_2$, $\text{CH}_2\text{NH}(\text{CH}_2)_2\text{CH}_3$, $\text{CH}_2\text{NHCO}_2\text{R}^4$, $\text{CH}_2\text{NHCH}_2\text{CH}_3$, CH_2NHCH_3 , $\text{NHCOC}(\text{CH}_3)_2$, or $\text{N}(\text{S}(\text{O})_2\text{CH}_3)_2$ substituent;

R^1 is hydrogen, halo, R^4 , CN , $\text{C}(\text{NOH})\text{R}^3$, $\text{C}(\text{NO}-\text{R}^4)\text{R}^3$, $(\text{CH}_2)_n\text{CO}_2\text{R}^4$, $(\text{CH}_2)_n\text{OR}^3$, COR^3 , CF_3 , SR^4 , $\text{S}(\text{O})\text{R}^4$, $\text{S}(\text{O})_2\text{R}^4$, $\text{COCH}_2\text{CO}_2\text{R}^3$, $\text{NH}\text{SO}_2\text{R}^4$, NHCOR^3 , $\text{C}(\text{NOR}^3)\text{NH}_2$, CH_2OCOR^3 , $(\text{CH}_2)_n\text{NH}_2$, $\text{CON}(\text{CH}_3)_2$, $(\text{CH}_2)_n\text{NHCO}_2\text{R}^4$, CO_2R^3 , CONH_2 , CSNH_2 , $\text{C}(\text{NH})\text{NHO}\text{R}^3$, $(\text{CH}_2)_n\text{N}(\text{CH}_3)_2$, or CONHNHCOR^3 ;

R^2 is 1,2-ethenediyl or 1,2-ethynediyl;

R^3 is hydrogen or C_1 - C_4 alkyl;

R^4 is C_1 - C_4 alkyl; and

n is 0, 1, 2, 3 or 4;

or a pharmaceutically acceptable salt thereof; or an N-oxide thereof.

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/4406 A61K31/44 C07D213/16 C07D213/18 C07D213/85
C07D213/89 C07D213/61 C07D213/65 A61P25/28 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, WPI Data, PAJ, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	✓ WO 01/90101 A (AVENTIS PHARMACEUTICALS PRODUCTS INC; ASTLES, PETER, C; EASTWOOD, PAUL) 29 November 2001 (2001-11-29) see page 161, line 4	5,6, 10-12, 18,20
X	✓ HOEKSTRA ET AL: "Potent, Orally Active GPIIb/IIIa Antagonists Containing a Nipecotic Acid Subunit. Structure-Activity Studies Leading to the Discovery of RWJ-53308" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 42, no. 25, 1999, pages 5254-5265, XP002142349 ISSN: 0022-2623 see 18a, scheme 5	5,6, 10-13, 18,20

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

14 June 2005

Date of mailing of the international search report

27.07.05

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	✓ WO 96/01825 A (FUJISAWA PHARMACEUTICAL CO., LTD; HEMMI, MITSUE +HF; SHIMAZAKI, NORIHI) 25 January 1996 (1996-01-25) see preparation 101,102, pages 133,134 and formula XIIB, page 18 -----	5-10,12, 13,15, 19,20
X	✓ WO 97/24355 A (FUJISAWA PHARMACEUTICAL CO., LTD; SHIMAZAKI, NORIHIKO; SAWADA, AKIHIKO) 10 July 1997 (1997-07-10) see preparation 2, page 47 and preparation 6, page 49 -----	5-10,12, 15,19,20
P,X	✓ SORENSEN U S ET AL: "Copper-free palladium-catalyzed sonogashira-type coupling of aryl halides and 1-aryl-2-(trimethylsilyl)acetylenes" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 61, no. 10, 7 March 2005 (2005-03-07), pages 2697-2703, XP004756737 ISSN: 0040-4020 see compound 2, Table 1, compounds 15,16 page 2700 -----	5-7,10, 12,19,20
X	✓ NOVAK, ZOLTAN ET AL: "Tandem Sonogashira coupling: An efficient tool for the synthesis of diarylalkynes" ORGANIC LETTERS , 6(26), 4917-4920 CODEN: ORLEF7; ISSN: 1523-7060, 12 February 2004 (2004-02-12), XP002331794 see pages 5,7,8 -----	5-10,12, 16,19,20
P,X	✓ WOLF, CHRISTIAN ET AL: "Palladium-phosphinous acid-catalyzed Sonogashira cross-coupling reactions in water" ORGANIC & BIOMOLECULAR CHEMISTRY , 2(15), 2161-2164 CODEN: OBCRAK; ISSN: 1477-0520, 30 June 2004 (2004-06-30), XP002331795 see Table 2, compounds 18,20 -----	5-10,12, 16,19,20
P,X	✓ HE H ET AL: "Copper-catalyzed cross-coupling of aryl iodides and aryl acetylenes using microwave heating" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 45, no. 16, 12 April 2004 (2004-04-12), pages 3237-3239, XP004498987 ISSN: 0040-4039 see entry o, table 1, page 3238 -----	5-8,10, 12,19,20
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>✓PENNEY J M ET AL: "Alkynylation of benzonitriles via nickel catalyzed C-C bond activation" TETRAHEDRON LETTERS, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 45, no. 25, 14 June 2004 (2004-06-14), pages 4989-4992, XP004510991 ISSN: 0040-4039 see entry 6, Table 1</p> <p>-----</p>	5-10,12, 16,19,20
P,X	<p>✓SUN, SHIH-SHENG ET AL: "Directed Assembly of Transition-Metal-Coordinated Molecular Loops and Squares from Salen-Type Components. Examples of Metalation-Controlled Structural Conversion" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY , 126(20), 6314-6326 CODEN: JACSAT; ISSN: 0002-7863, 2004, XP002331796 see page 6315 experimental3-tbu-5-(3'-ethynylpyridyl)-2-OH benzaldehyde</p> <p>-----</p>	5-8,10, 12,19,20
X	<p>✓RAJADURAI, CHANDRASEKAR ET AL: "Study on the Heteroatom Influence in Pyridine-Based Nitronyl Nitroxide Biradicals with Phenylethynyl Spacers on the Molecular Ground State" JOURNAL OF ORGANIC CHEMISTRY , 68(26), 9907-9915 CODEN: JOCEAH; ISSN: 0022-3263, 2003, XP002331797 se compound 10, figure 2</p> <p>-----</p>	5-8, 10-12, 18-20
X	<p>✓KATRITZKY, ALAN R. ET AL: "The preparation of diarylacetylenes via diphenyl (benzotriazol-1-yl)(aryl)methylphosphonates" ARKIVOC (GAINESVILLE, FL, UNITED STATES) , (13), 17-27 CODEN: AGFUAR URL: HTTP://WWW.ARKAT-USA.ORG/ARK/JOURNAL/2002/KARABATSOS/GK-706F/706F.PDF, 2002, XP002331798 see entry 11, Table 2 and experimental, page 26, last compound</p> <p>-----</p>	5-10,12, 19,20
X	<p>✓WO 03/035620 A (ASAHI KASEI KABUSHIKI KAISHA; MIYOSHI, SHIRO; OGAWA, KOHEI) 1 May 2003 (2003-05-01) see reference example 9A & EP 1 447 400 A (ASAHI KASEI PHARMA CORPORATION) 18 August 2004 (2004-08-18)</p> <p>-----</p>	5-8,10, 12,16, 19,20
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	✓WANG, ZHIYONG ET AL: "An improved coupling reaction for the preparation of pyridylethynyl benzonitrile compounds" CHINESE SCIENCE BULLETIN , 46(19), 1606-1608 CODEN: CSBUEF; ISSN: 1001-6538, 2001, XP009048572 see compounds 6a,6c -----	5-10,12, 19,20
X	✓LIN, WENBIN ET AL: "Three-Dimensional Manganese(II) Coordination Polymers Based on m-Pyridinecarboxylates: Synthesis, X-ray Structures, and Magnetic Properties" INORGANIC CHEMISTRY , 39(18), 4169-4173 CODEN: INOCAJ; ISSN: 0020-1669, 2000, XP002331799 see page 4169, Scheme 1, last line page 4170 and reference 22 -----	5-8,10, 12,16, 19,20
P,X	✓CRYSTAL GROWTH AND DESIGN, <i>ART</i> vol. 5, no. 2, <i>MAULIK</i> 14 September 2004 (2004-09-14), pages 609-616, XP002331800 see compound 3 page 610 -----	5-7,9, 10, 12-14, 19,20
X	✓EP 0 436 398 A (ALLERGAN, INC) 10 July 1991 (1991-07-10) cited in the application see formula I definitions -----	5
A	✓WO 01/16121 A (MERCK & CO., INC; COSFORD, NICHOLAS, D., P; MCDONALD, IAN, A; BLEICHER) 8 March 2001 (2001-03-08) cited in the application the whole document -----	1-25
A	WO 01/72291 A (THE VICTORIA UNIVERSITY OF MANCHESTER; BROTHIE, JONATHAN; HILL, MICHA) 4 October 2001 (2001-10-04) cited in the application the whole document -----	1-25
P,A	✓WO 2004/067002 A (RECORDATI S.A; RECORDATI INDUSTRIA CHIMICA E FARMACEUTICA S.P.A) 12 August 2004 (2004-08-12) see formula I -----	1-25

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Information on patent family members

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